Remarks

The claim of domestic priority has been updated to include the patent number of the immediate parent of the subject application.

Claims 1-2, 5, 27, 37, 47, 52, and 61 were objected to because of lack of the indefinite article. These claims have been amended to use the indefinite article.

The rejection of claims 1, 5, 27, 37-39, and 61-62 under 35 U.S.C. § 112, first paragraph, and claims 5, 52, 53, and 55 under 35 U.S.C. § 112, second paragraph

Claims 1, 27, 37-39 stand rejected for alleged lack of adequate description and for alleged lack of enablement. The step of treating was said to be too broad relative to the disclosure provided. The phrase "treating with a vascular permeability agent" was suggested as being of the proper scope. The claims have been amended to recite "contacting with an agent which increases vascular permeability." It is respectfully submitted that the specification indeed provides an adequate written description and enablement for a step of such scope.

In the body of the rejection, claims 5, 61, and 62 are also mentioned as not enabled for the term "low calcium concentration." See Paper 200401 at page 5, third paragraph. This phrase has been replaced with specific recited concentrations of calcium: "less than or equal to 500 micromolar calcium," "about 500 μmol/L or less," or "about 40 μmol/L to about 500 μmol/L." A similar issue is raised under the guise of 35 U.S.C. § 112, second paragraph for claims 5, 52, 53, and 55. As mentioned above, the offending phrase has been clarified with particular recited concentrations.

It is respectfully submitted that the clarifying amendments have addressed these issues and obviated the rejections.

The rejection of claims 1, 2, 47 and 52 under 35 U.S.C. § 102(a)

Claims 1, 2, 47 and 52 are rejected as anticipated by Fasano (WO 96/37196). Fasano is cited for teaching the use of a vascular permeability agent and a nucleic acid. However, Fasano does not teach the use of a calcium concentration of less than or equal to 500 micromolar as required by each of claims 1, 47 and 52. Thus Fasano does not anticipate claims 1, 47 or 52.

The rejection of claims 1, 2, 47 and 52 under 35 U.S.C. § 102(e)

Claims 1, 2, 47 and 52 are rejected as anticipated by Wolff (U.S. 6,265,387). Wolff is cited for teaching the use of a VEGF to enhance vascular permeability and a nucleic acid. However, Wolff does not teach the use of a calcium concentration of less than or equal to 500 micromolar as required by each of claims 1, 47 and 52. Thus Wolff does not anticipate claims 1, 47 or 52.

The rejection of claims 1, 2, 37, 47, and 52 under 35 U.S.C. § 102(e)

Claims 1, 2, 37, 47, and 52 are rejected as anticipated by Ryan (US 2003/0195495 A1). Ryan is cited for teaching the use of a combination of VEGF, vascular permeability agent and a nucleic acid encoding VEGF. However, Ryan does not teach the use of a calcium concentration of less than or equal to 500 micromolar as required by each of claims 1, 37, 47 and 52. Thus Ryan does not anticipate claims 1, 37, 47 or 52.

The rejection of claims 1, 2, 27, 28, 47 and 52 under 35 U.S.C. § 103(a)

Claims 1, 2, 27, 28, 47 and 52 are rejected as obvious over Nabel (U.S. 5,328,470) taken with Wolff (U.S. 6,265,387), Epstein (U.S. 6,007,817), or Neufeld (U.S. 6,013,780). This rejection is respectfully traversed.

Nabel is cited for teaching a nucleic acid delivery kit comprising a catheter and DNA encoding a toxin. Wolff, Epstein, and Neufeld are each cited as disclosing a vascular permeability agent for enhancing the delivery of a bioactive molecule. The combination of these teachings would allegedly have been obvious.

To make a proper *prima facie* case of obviousness, the references must teach all elements of the rejected claims.

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

M.P.E.P. § 2143. Each of the rejected claims requires a low calcium concentration. None of the cited references teaches the use of low calcium concentration to enhance DNA delivery. Since the combination of references fails to teach all elements of the rejected claims, the rejection fails. Withdrawal of this rejection is respectfully requested.

The rejection of claims 37-39 under 35 U.S.C. § 103(a)

Claims 37-39 are rejected as obvious over Ryan taken with Wolff, Epstein, or Neufeld. This rejection is respectfully traversed.

The rejection posits that it would have been obvious to modify the DNA delivery method of Ryan by employing a vascular permeability agent so as to enhance the delivery of DNA to target cells *ex vivo*.[1] Wolff, Epstein, or Neufeld are cited as teaching vascular permeability agents. However, the cited references do not teach the delivery of DNA under conditions of low calcium as required by the claims. Thus the cited combination of references fails to each all elements of the claims, and thus the cited combination fails to present a *prima facie* case of obviousness.

Withdrawal of the rejection is respectfully requested.

The rejection of claims 1, 2, 5, 27-28, 47-48, 52-56, 61-75 under the judicially created doctrine of obviousness-type double patenting

A terminal disclaimer is submitted to obviate any double patenting issues.

[1] Claims 37-39 does not specify *ex vivo* delivery. The DNA delivery can also be done *in vivo* in a donor. The cells are removed and transplanted to a recipient. The specification teaches at page 6, lines 7-20: "More particularly, the exogenous nucleic acid can be administered in vivo or ex vivo to donors cells or organs, e.g. a xenogeneic heart, liver, spleen and the like, in accordance with the invention and the donor cells or organ can be transplanted to a selected host, e.g. a mammal, particularly a primate such as a human."

Respectfully submitted,

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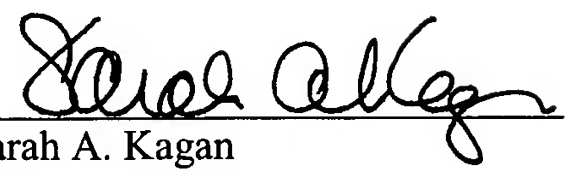
By: 

Sarah A. Kagan
Registration No. 32,141

Banner & Witcoff, Ltd.
Customer No. 22907